REMARKS

Claims 383 and 384 stand rejected under 35 U.S.C. §112, second paragraph, as failing to satisfy the definiteness requirement of the statute. Specifically, the Examiner posits that the specification fails to provide a "definition setting forth the metes and bounds" of the questioned "multifactorial and nonspecific" language. Basis for this rejection is said to exist at page 5 of the Office Action mailed 03 June 2004. Applicant disagrees that the claims fail to satisfy the second paragraph requirement of the statute for the following reasons.

The Examiner concludes on page 4 of the 21 June Action that while the specification at pages 37, line 19 and page 50, lines 2 and 3 describes "multifactorial and nonspecific cells" as comprising "stem cells and germinal cells" and as having "pluripotent" characteristics, such description does not define the "metes and bounds" of the questioned language. The Examiner has proffered no sound reasoning in support of her conclusion. Rather, the reasoning applied by the Examiner in the Section 102 grounds of rejection (which recognizes the ability of multifactorial and non-specific cells to "give rise to all of the cell types") appears to express an understanding that is inconsistent with and contrary to the reasoning upon which this Section 112 technical ground of rejection was based. It appears that the Examiner's anticipation rejection was bottomed on an understanding of the multifactorial and non-specific roles characteristic of pluripotent stem cells. Applicant believes that the Examiner's reasoning expressed in the Section 102 rejection is the correct understanding of Applicant's disclosure, which should render any question of indefiniteness moot.

Initially, Applicant points out that the Examiner's statement that, "Stem cells are at least pluripotent" evinces a misunderstanding in regard to cell biology because all stem cells are not pluripotent. Only nonspecialized stem cells, which possess the characteristics that enable such cells to be not fixed as to developmental potentialities, are defined as pluripotent. Clearly, it is

well understood by those skilled in the art that all stem cells do not possess pluripotent characteristics.

Page 37, line 19 of Applicant's specification defines "multifactorial and non-specific cells" as stem cells and germinal cells. Page 48, lines 13-15, discloses that, "if germinal cells (and in some cases, stem cells) are utilized a direct differentiation and morphogenesis into an organ can occur..." An organ is defined on page 44, lines 12-18 of Applicant's specification as consisting "of two or more kinds of tissues joined into one structure that has a certain task." In addition, page 50, lines 2-5 define "multifactorial and non-specific" growth factors as being "pluripotent." Applicant believes that one skilled in the medical art, including declarants Drs. Heuser and Lorincz, based upon the above portions of the specification, would understand the meaning and intended scope of "multifactorial and non-specific."

On page 4 of the 21 June Action, referring to the disclosure at page 37, line 19, the Examiner stated that examples of what the term encompasses "does not constitute a definition setting forth the metes and bounds of the phrase." However, the Examiner failed to specifically identify why one skilled in the art based on the totality of the record, including Applicant's submissions and declaration evidence, would find Applicant's disclosure nondescriptive of the metes and bounds of the claimed invention. Furthermore, Applicant is not required to provide a definition for terms that are well known by those skilled in the art.

It is clear from a reading of the instant specification that the qualities and characteristics of multifactorial and non-specific cells can be found in pluripotent cells such as stem cells and germinal cells. No one skilled in the art would seriously question that a fundamental property of all of these cells is that they are undifferentiated. Also, no one skilled in the art would question that "pluripotent" cells are undifferentiated stem cells, which are highly versatile and can give

rise to the growth of multiple tissues. Dr. Elia recognized that such versatility results from their uniquely unspecialized condition, which allows such cells to be used to carry out the non-specific tissue function disclosed and claimed in the subject application for integrally growing soft tissue, including a new artery in a human patient.

Applicant disagrees with the Examiner's criticism in regard to the information contained in Exhibit D in the Appeal Brief submitted on 12 April 2005 and received by the PTO on 15 April 2005 (receipt of which was acknowledged by the Examiner on page 3 of the 21 June Action). Applicant submitted this document to establish that the unique versatile and nonspecialized characteristics of pluripotent cells were known to workers in the art. Applicant employed the criticized language to define a genus of cells that are characterized by having the capacity to promote the growth of all three major soft tissue types, i.e., pluripotent cells.

As succinctly pointed out above, Applicant has used "multifactorial and non-specific" to describe or characterize the pluripotent potentialities of stem cells and germinal cells. Applicant believes that the PTO should take Official Notice of the fact that the term "pluripotent" is well known to those in the medical art to describe versatile cells whose plasticity renders them uniquely capable of effecting growth of more than one type of tissue in the body. Those skilled in the medical art would understand from Applicant's disclosure that multifactorial and non-specific cells can be a germinal cell (page 48, lines 6-8) or a stem cell (page 48, lines 13-15). However, not all stem cells are multifactorial and non-specific. Multifactorial and non-specific stem cells have the necessary plastic characteristics to promote growth of various types of soft tissue, including a new artery. On pages 4 and 5 of the 21 June Action, the Examiner states that, "The crux of the issue is what cells other than stem cells can be considered multifactorial and nonspecific?" The Examiner has already answered her own question (in the same paragraph in

which the question was raised) by again referring to the instant specification at page 37, line 19, where it is set forth that, in addition to stem cells, multifactorial and non-specific cells may also include germinal cells. Accordingly, Applicant is at a loss to understand why the Examiner fails to comprehend that the subject specification used such language to characterize a genus of cells that exhibit pluripotent characteristics. Cells that do not exhibit such pluripotent characteristics cannot provide the integrated soft tissue growth required by the subject claims and are excluded from the scope of the claimed invention.

Moreover, as pointed out above, an applicant is not required to define well-known medical terminology that would be readily understood by one skilled in the art. Additional confirmation of such understanding by one skilled in the art may be found in the Second Supplemental Declarations of Drs. Richard Heuser and Andrew C. Lorincz, at paragraphs 6 and 10 of such Declarations, which state that cellular growth factors described and claimed in the subject application are understood to include multifactorial and non-specific cells. Apparently, the declarants, after reading the pertinent text of the subject application, did not view the questioned language to be unclear. It was error for the Examiner to fail to weigh the evidentiary value of these declarations because they relate to the meaning of the questioned language.

In summary, one skilled in the medical art would understand that Applicant's above description of multifactorial and non-specific cells as including pluripotent stem cells and germinal cells is consistent with the knowledge of the art and would have no difficulty in understanding the scope of protection sought by the claims. On page 4 of the 21 June Action, the Examiner acknowledges that the specification "establishes that **one of the features** of a 'multifactorial and nonspecific' growth factor (wherein a 'growth factor' is defined in the specification as encompassing cells) is that it is pluripotent." Applicant submits that such

descriptive language, in and of itself, when viewed by one skilled in the art suffices to establish the scope of said term. The purpose of the second paragraph requirement of 35 U.S.C. §112 is to ensure due process of law, i.e., to give notice to the public as to the metes and boundaries adhering to patent claims. In re Hammack, 427 F.2d 1378, 166 USPQ 204 (CCPA 1970). Accordingly, the Examiner's rejection of the language contained in claims 383 and 384 under 35 U.S.C. §112, second paragraph, for indefiniteness must fail for lack of a sound factual basis.

Claims 382-388 were rejected under 35 U.S.C. §112, first paragraph, for failing to comply with the written description requirement. The Examiner considered that the specification only used the word "bud" in reference to tooth buds and that tooth buds do not form soft tissue, including arteries, as required by the claims, apparently implying that the description of the invention contained no basis for buds that form soft tissue. As will be more fully set forth below, Applicant believes that such rejection is based upon an erroneous technical understanding and that one skilled in the art would readily understand that buds for growing soft tissue are a part of Applicant's invention. Applicant further believes that as a consequence, the claimed invention is described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the Applicant, at the time the application was filed, had possession of the claimed invention.

First of all, Applicant's specification describes growth of soft tissue, such as arteries (page 45, line 1 to page 46, line 16) with the placement of cells into the body of the patient. The Examiner admits at page 8, lines 9 and 10 of the 21 June Action, that vasculature [sic] soft tissue inherently forms from buds. Thus, the growth and formation of an artery, by the Examiner's own admission, must necessarily go through a bud stage. Such inherent disclosure would be well understood by one skilled in the art and thus reasonably describes that a bud is necessary for

the growth of an artery. Applicant believes that the Examiner's admission is sufficient to resolve this issue and to overcome the rejection.

Secondly, the Examiner stated at page 9 of the 21 June Action that, "The specification only uses the term "bud" in reference to tooth buds. Tooth buds do not form soft tissue, including arteries, as required by the claims." The above statement is erroneous because the growth of a tooth from a tooth bud involves the growth of both hard and soft tissue. Official Notice may be taken of the fact that arteries and veins are necessary and vital components of a tooth. In any event, The Merck Manual of Health & Aging, Section 3, Chapter 39, entitled "Tooth Decay" found at http://www.merck.com (attached hereto as Exhibit A) states that the interior of a tooth consists of dentin and pulp and that the pulp contains the nerve, artery, and vein of each tooth. As further illustration, The World Book Encyclopedia, 2005 Edition, at page 81 of Volume 19 (attached hereto as Exhibit B) verifies in the drawing that an artery and a vein are part of a tooth. These publications further support the fact that the instant specification reasonably describes to those skilled in the art that a bud subsequently forms soft tissue, such as an artery or vein.

The Examiner's attention is further directed to the Declarations of Drs. Andrew E. Lorincz, Wayne H. Finley, and C. Gene Wheeler (of record). While these Declarations speak for themselves, it is evident that all three declarants believed that the relied upon portion of the Applicant's specification related to a method for forming a bud and resulting soft tissue at a desired site in a body. Specific attention is directed to Paragraphs 3-5 of the respective Declarations. Obviously, these eminent physicians determined that the questioned language is described in the originally filed application. The decision in In re Alton, 76 F.3d 1168, 37 USPQ 2d 1578 (Fed. Cir. 1996) is supporting authority that the PTO must weigh expert evidence in

determining compliance with the "written description" requirement of the statute. In the instant situation, Applicant believes that the Examiner must accord strong evidentiary weight to the Declarations, especially when it is considered that the three Declarations were submitted years in advance of this newly raised issue.

In view of the above three paragraphs, it is clear to one skilled in the art that Applicant's specification reasonably describes a bud for growing soft tissue. Applicant observes that the rejection appears to be based upon a hyper technical application of 35 U.S.C. §112, first paragraph, which should be withdrawn in view of the interpretation given this statutory requirement in a line of decisions exemplified by In re Robins, 429 F.2d 452, 166 USPQ 552 (CCPA, 1970); In re Borkowsky, 422 F.2d 904, 164 USPQ 642 (CCPA, 1970); and In re Wakefield, 422 F.2d 897, 164 USPQ 636 (CCPA, 1970).

Applicant submits that claims 382-394 are described in such manner that one skilled in the art would understand that a bud was reasonably described for both hard and soft tissue. Accordingly, the Examiner is requested to favorably reconsider and withdraw the rejection under 35 U.S.C. §112, first paragraph.

Claims 382-388 stand rejected under 35 U.S.C. §102(b) as anticipated by Lutjen. The Examiner has posited that the *in vitro* fertilization reported by Lutjen responds to the claimed method of implanting cells in a human patient. Applicant believes that the Examiner's reasoning is critically flawed and must fail for lack of sound evidentiary basis for the following reasons.

Before turning to the rejection involving claims 382-388 under 35 U.S.C. §102, Applicant believes that an understanding of the remarks concerning such rejection would be facilitated by a review of certain basic medical terminology relating to cell biology.

The National Institutes of Health (hereinafter "NIH"), on its website, http://www.nlm.nih.gov/medlineplus/mplusdictionary.html defines three types of stem cells, i.e., totipotent, pluripotent, and unipotent (attached hereto as Exhibit C) as follows:

Totipotent: Capable of developing into a complete organism or differentiating into any of its cells or tissues.

Pluripotent: Not fixed as to developmental potentialities.

Unipotent: Capable of developing only in one direction or to one end product.

Totipotent cells, such as the two-cell embryo disclosed in Lutjen, are capable of developing into a complete organism such as a human being by differentiating into any of the cells or tissues of such human being. Accordingly, totipotent cells, unlike pluripotent cells, are fixed as to developmental potentialities, i.e., the formation of a human being. Pluripotent cells do not have the ability to form a multicellular human organism. Unipotent cells are capable of developing into only one tissue type. When these definitions are understood and utilized in connection with the rejections under 35 U.S.C. §102, it will become apparent that this rejection should be withdrawn.

Several additional points remain regarding terminology utilized in cell biology. First, the Examiner used the term, "omnipotency" at page 5 of the 21 June Action. The word "omnipotent" was searched on the above-mentioned NIH website, and no matching entries were found. Perhaps, the Examiner intended to use the term "totipotent." In any event, the Examiner appears to indicate that such cells are able to differentiate into any cell type. The Examiner questioned, at page 5 of the 21 June Action, whether "nonspecific" means that a cell must be able to

differentiate into any cell type or just more than one. In the context of Applicant's specification, a non-specific cell has the potential to differentiate into multiple cell types and is not limited to a single cell type. In addition, the Examiner stated at page 4 of the 21 June Action that, "Stem cells are at least pluripotent." Such statement is also viewed as being at variance with the above-cited NIH definitions because, as demonstrated above, not all stem cells are pluripotent. Applicant believes that the language of the subject claims would be interpreted and understood by one skilled in the art by reading the specification and by referring to the well-accepted and unambiguous terminology published by the NIH. Certainly, Applicant's description of pluripotent cells as set forth in the instant specification is consistent with the definition published by the NIH.

Claim 382 was amended to make explicit what was already implicit in the claim by adding that the grown soft tissue produced by the method of the invention is integrated into the body of the patient. Claim 382 was further amended to recite that the produced and integrated soft tissue was at a selected site in the body of the patient and that the bud was formed at such selected site. This amendment makes it clear that such growth and integration occurred in the previously claimed "in a body of a human patient," not in a fetus that develops from an embryo. Antecedent basis for "integrated" can be found in Applicant's specification at page 54, lines 7-17; page 56, lines 14-19; page 61, lines 23-30; and page 62, lines 2-10. Antecedent basis for "a selected site" can be found in Applicant's specification at least at page 21, lines 10-13; page 31, lines 22 and 23; page 32, lines 9-11; and page 45, lines 1-4 and 27-30. In any event, the additional claim language "integrating" and "selected site" removes any possible ambiguity as to where the bud and resultant soft tissue are grown.

With the above information and discussion in mind, Applicant will now more specifically address the rejection under 35 U.S.C. §102.

The two-cell embryo utilized by Lutjen for *in vitro* fertilization is totipotent and, as such, can only result in formation of a multicellular human organism. Accordingly, the cells implanted by Lutjen and Applicant require distinct starting materials, which necessarily produce distinct end products. A two-cell embryo consists of totipotent cells, which are considered the "master cells" of the body because they contain all the genetic information needed to create all the cells of the human body plus the placenta, which nourishes the human embryo. It is the ability to create the placenta, which forms a barrier allowing only gas exchange between the developing conceptus and the human host that clearly distinguishes the two-cell embryo implanted by Lutjen from the cells disclosed and claimed by Applicant.

While the Examiner purports to give the claimed language its "broadest reasonable interpretation," Applicant points out that the interpretation foisted by the Examiner patently fails the test for reasonableness. During prosecution, it is proper for the PTO to apply to "verbiage of the proposed claims the broadest reasonable meaning of the words in their ordinary usage as they would be understood by one of ordinary skill in the art, taking into account whatever enlightenment by way of definitions or otherwise may be afforded by the written description contained in the applicant's specification." In re Morris, 127 F.3d 1048, 1054-55, 44 USPQ 2d 1023, 1027-28 (Fed. Cir. 1997). The Examiner has not pointed to a definition, specific disclosure, or any other pertinent information in the subject specification that either explicitly or implicitly teaches or infers that Applicant's novel method of integrally growing soft tissue in a human patient encompasses implanting an embryo to grow a multicellular human organism. Rather, the description of Applicant's invention in the specification is directed to placing cells in

the body of a human patient to grow soft tissue, which integrates itself with existing tissue in the patient. To continue to interpret the specification disclosure in the manner proposed by the Examiner would be repugnant to such integrated tissue growth and would epitomize unreasonableness rather than reasonableness. It is well established that claims are to be interpreted in light of the specification, and the Examiner should so further interpret the amended and newly presented claims.

In summary, there clearly exists a difference in kind between the cells implanted by Applicant's invention, which result in growing and integrating soft tissue in the body of a human patient as described and claimed herein, and the embryo implanted in a human to accomplish *in vitro* fertilization for growing a multicellular human organism that ultimately develops into a separate functional entity. Simply stated, because the potential of pluripotent cells is not total, such cells are not totipotent and are not embryos. To contend otherwise defies science, as well as logic.

As noted earlier, claim 382, as amended, explicitly requires that the soft tissue grown from the bud is grown and integrated at a selected site in the human patient's body. Moreover, amended claim 382 clearly defines novel subject matter by excluding the placenta-encased fetus resulting from the embryo implantation and developing conceptus reported by Lutjen, which embodies the development of a separate and ultimately independent multicellular human organism. Applicant believes that it would be unreasonable and illogical to assert that the soft tissue of a developing fetus becomes integrated in the body of the host patient.

New dependent claims 389-394 further define novel subject matter by limiting the type of cells placed in the patient's body to form buds and limiting the type of soft tissue grown from such buds.

Applicant submits that amended claims 382–394 define novel subject matter within the purview of 35 U.S.C. §102, and favorable reconsideration of the rejections of record is respectfully requested.

From the foregoing amendment to the claims and accompanying remarks, Applicant submits that the instant application is in condition for allowance, and a Notice to such effect is respectfully requested. Should the Examiner have any questions or require additional information or discussion to place the application in condition for allowance, a phone call to the undersigned attorney would be appreciated.

Respectfully submitted,

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